REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-15, as well as newly added Claims 21 to 23, the only claims pending and currently under examination in this application.

Claims 1 and 5 have been amended to remove certain language and specify that the reaction is a cyclic reaction that produces linearly amplified amounts of nucleic acids, support for this amendment being found at page 11, line 4. New Claims 21, 22 and 23 are separate independent versions of Claim 1 and Claims 4 and 9. Accordingly, this amendment introduces no new matter and its entry by the Examiner is respectfully requested.

The Examiner is thanked for the interview held on February 25, 2004. The Examiner's summary of the interview is complete and correct.

Objection under 35 U.S.C. § 132 and rejection under 35 U.S.C. § 112, first paragraph

The Office Action maintains the Examiner's position that the amendment filed September 3, 2002 contains new matter pursuant to 35 U.S.C. § 132 and does not comply with the requirements of 35 U.S.C. § 112, 1st ¶. Soley in order to expedite prosecution of the present application and without in anyway agreeing with the Examiner's position, the claims have been amended to remove the objected to phraseology. Accordingly, this objection and rejection may be withdrawn.

Rejection of Claims 5-9 under 35 U.S.C. § 112, second paragraph

Claims 5 to 9 have been rejected under 35 U.S.C. § 112, 2nd ¶ for an asserted lack of clarity with respect to the presence or absence of linking group L. It is respectfully submitted that, in view of the claim language as a whole and the

specification, one of skill in the art would clearly know that L is optional, and that in those embodiments where L is not present, the formulate would read: surface-L-R-F-cV-5'. As such, it is submitted that this rejection may be withdrawn.

Rejection of Claims 1-15 under 35 U.S.C. § 102(e) over Wolber

Claims 1-15 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Wolber.

In making this rejection, the Examiner asserts that Wolber teaches an array of probe nucleic acid having a constant domain "polyA" and a variable domain which is the coding region, and that this array is employed to produce a template array of overhang nucleic acids, **which in turn is then subjected to a primer extension reaction**. The Examiner cites to Columns 6 and 13 in support of this reading.

However, it is respectfully submitted that this reading is incorrect. In Column 6, the recited step is an entirely solution-phase step to produce oligonucleotide tagged nucleic acids. In other words, Column 6 is directed to a solution phase protocol to produce oligonucleotide tagged nucleic acids, where an array is never employed. As such, an array is not employed in this step and not subjected to linear PCR.

The only time an array is employed in the method disclosed in Wolber is to detect already made tagged nucleic acids. **When the array is contacted with the oligonucleotide tagged nucleic acids, it is not then subjected to a further reaction, such as linear PCR, as required by the claims**.

Accordingly, contrary to the characterization of Wolber by the Examiner, Wolber never teaches subjecting a template array to a reaction such as linear PCR.

Therefore, Wolber fails to anticipate the claimed invention and this rejection may be withdrawn.

Rejection of Claims 1-4 under 35 U.S.C. § 102(b) over Bulyk

The Examiner has next maintained the rejection of Claims 1-4 under 35 U.S.C. § 102(b) as being anticipated by Bulyk. In maintaining this rejection, the Examiner asserts the phrase "comprising" means the recited singled stranded product could in fact be double stranded. This comprising phrase has now been removed from the claims.

As previously reviewed, Bulyk teaches a method of cleaving surface immobilized double stranded (ds) structures using restriction endonucleases, which produces a mixture of ds nucleic acids. The claims now specify that the reaction employed is one that is cyclic, or a reaction clearly not taught by Bulyk. As such, Bulyk does not anticipate the claims which are directed to a use of a cyclic reaction or a specific reaction not taught by Bulyk. Accordingly, this rejection may be withdrawn.

Rejection of Claims 5-6 and 8-9 under 35 U.S.C. § 103(a) over Bulyk

Claims 5-6 and 8-9 have next been rejected under 35 U.S.C. § 103(a) as being obvious over Bulyk. In maintaining this rejection, the Examiner asserts that the transitional term comprising does not exclude the ds product of Bulyk. However, the claims are now limited to methods that employ a cyclic reaction, which reaction is clearly not taught or suggested by Bulyk. Accordingly, this rejection may be withdrawn.

Rejection of Claims 7 under 35 U.S.C. § 103(a) over Bulyk in view of Dattagupta

Claim 7 has next been rejected under 35 U.S.C. § 103(a) as being obvious over Bulyk in view of Dattagupta. In maintaining this rejection, the Examiner asserts that the transitional term comprising does not exclude the ds product of Bulyk. However, the claims are now limited to methods that employ a cyclic reaction. Bulyk teaches a primer extension method that includes cleaving surface immobilized ds structures using restriction endonucleases, which produces a mixture of ds nucleic

acids. As such, Bulyk does not teach or suggest a method that employs a cyclic reaction. As Dattagupta has been cited solely for the element of an RNA polymerase, this secondary reference cannot make up the above-described fundamental deficiency in Bulyk. Accordingly, this rejection may be withdrawn.

Rejection of Claims 10 to 15 under 35 U.S.C. § 103(a) over Bulyk in view of Cantor

Claims 10-15 have next been rejected under 35 U.S.C. § 103(a) as being obvious over Bulyk in view of Cantor. In maintaining this rejection, the Examiner asserts that the transitional term comprising does not exclude the ds product of Bulyk. However, the claims are limited to methods that employ a cyclic reaction to produce single stranded nucleic acids. Bulyk teaches a primer extension method of cleaving surface immobilized ds structures using restriction endonucleases, which produces a mixture of ds nucleic acids. As such, Bulyk does not teach or suggest a method that employed a cyclic reaction to produce ss nucleic acids, and therefore does not make these claims obvious. As Cantor has been cited solely for the teaching of the use of the solution phase product in target generation, this secondary reference cannot make up the above described fundamental deficiency in Bulyk. Accordingly, this rejection may be withdrawn.

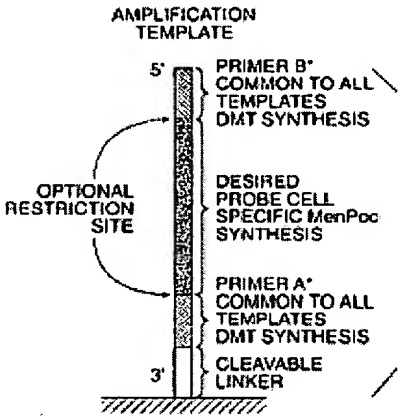
Rejection of Claims 1-6 and 8-9 under 35 U.S.C. § 103(a) over Lipshutz in view of Bulyk

Claims 1-6 and 8-9 have next been rejected under 35 U.S.C. § 103(a) as anticipated by Lipshutz (USPN 6,280,950) in view of Bulyk, assertedly because Lipshutz describes a primer extension reaction performed upon an array of nucleic acid probes that teaches all of the elements of the claimed methods but for the use of 5' variable domain, which is assertedly taught by Bulyk.

As previously explained, Lipshutz discloses a method for producing a mixture of nucleic acids involving an array of nucleic acid probes. The composition of Lipshutz probes is described in great detail in column 2 line 66 to column 3 line 35

and summarized in the first panel of Fig. 1 of the Lipshutz disclosure. This panel of Fig. 1 of the Lipshutz reproduced here for the Examiner's convenience.

First panel of Figure 1 of Lipshutz (USPN 6,280,950):



As can be seen from the figure, the Lipshutz probes contain regions at the 5' and 3' ends of the probes that are called "PRIMER B* COMMON TO ALL TEMPLATE DMT SYNTHESIS" and "PRIMER A* COMMON TO ALL TEMPLATE DMT SYNTHESIS", respectively. These regions are homologous to the constant regions of the probes recited in the instant claims. These probes are the only probes on Lipshutz' array, and, as such, Lipshutz only teaches an array containing probes containing constant regions at their 5' ends.

Even in view of Bulyk, one of skill in the art would not be motivated to modify the Lipshutz array to contain probes that have variable domains at their 5' ends since all of Lipshutz primer extension methods involve amplification reactions that require the presence of two constant domains as primer sites (e.g. non-linear PCR amplification). A variable domain placed on the 5' end of Lipshutz probes would not be amplifiable using Lipshutz' methods, and, as such, one of skill in the art would lack motivation to change Lipshutz' methods to teach the claimed method.

Bulyk fails to provide any such motivation because Bulyk only cleaves the ds nucleic acids to confirm that primer extension reactions were complete, and therefore would not be looked to by one of skill in the art as motivation to modify the Lipshutz method to use a 5' variable domain. Furthermore, if one were to modify Lipshutz in view of Bulyk, one would also have to include a cleavage step as taught by Bulyk, where the entire surface immobilized duplex structure is cleaved from the surface, which one negate the workability of Lipshutz' method.

Because the Lipshutz fails to teach an array containing probes that have constant domains at their 5' ends and one of skill in the art would not be motivated by Bulyk to modify Lipshutz to include a 5' variable domain, Claims 1-6 and 8-9 are not obvious over Lipshutz in view of Bulyk and this rejection may be withdrawn.

Rejection of claim 7 under 35 U.S.C. § 103

Claim 7 has been rejected under 35 U.S.C. § 103(a) as being obvious over Lipshutz and Bulyk and further in view of Dattagupta.

As established above, the combined teaching of Lipshutz and Bulyk is deficient in that it does not teach an array of probes containing variable domains at their 5' ends. This deficiency is not made up by Dattagupta's RNA polymerase, and cannot be met by knowledge available to one of skill in the art. As such, the combination of Lipshutz and Bulyk in view of Dattagupta cannot render the subject matter of Claim 7 obvious. Accordingly, this rejection may be withdrawn.

Rejection of Claims 10-15 under 35 U.S.C. § 103 over Lipshutz in view of Bulyk and further in view of Cantor

Claims 10-15 have been rejected under 35 U.S.C. § 103(a) as being obvious over Lipshutz and Bulyk in view of Cantor.

Each of Claims 10-15 involves the method of producing a mixture of nucleic acids recited in Claim1. As such, each of Claim 10-15 involves an array containing probes having variable domains at their 5' ends. Claims 10-13 further involve a target generation step in which target nucleic acids are produced from an mRNA sample. The target generation step requires a variable domain at the 5' end of the probes for a target to be generated.

As established above, the combined teaching of Lipshutz and Bulyk is deficient in that it fails to make obvious the claimed protocols of using an array containing probes that have variable domains at their 5' ends. As previously established above and in the Applicants' previous response, Lipshutz strongly teaches away from using probes that have a variable domain at their 5' ends since Lipshutz' primer extension methods involve amplification reactions that require the

presence of two constant domains acting as primer sites, and Bulyk is not concerned with making product nucleic acids for use in another application.

Cantor's methods of employing Lipshutz' mixture of nucleic acids fails to make up for the fundamental Lipshutz/Bulyk deficiency. As such, Lipshutz and Bulyk in combination with Cantor fails to teach or suggest the claimed invention and this rejection may be withdrawn.

CONCLUSION

The applicant respectfully submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Gordon Stewart at 650 485 2386. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: 3/24/04

By: _____
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